REMARKS

Applicants have amended claim 1 to recite that the virus composition is frozen at a rate of -0.5°C to -2.5°C per minute. Support for this amendment can be found throughout the specification as filed, *e.g.*, at paragraph [0058]. Applicants also have amended claim 1 to recite that the lyophilized virus composition has less than about a 17.6% log PFU loss after at least one year at a storage temperature of about 1°C to about 10°C. Support for this amendment can be found throughout the specification as filed, *e.g.*, at Table 7.

None of these amendments introduces new matter.

Upon entry of these amendments, claims 1, 3, 5, 6, 8, 11, 13, 18, 22-25, 30, 33, 35, 37, 41-43, 46, 48-50, 54, 55, 60-63, 86, 105, and 122-124 will be pending in the application. Of these, claims 43, 46, 48-50, 54, 55, 60-63, 86, 105, and 122-124 are withdrawn.

THE REJECTIONS

35 U.S.C. § 112

Claims 1, 3, 5, 6, 8, 11, 13, 22-25, 30, 33, 35, 37, 41, and 42 stand rejected under 35 U.S.C. § 112, second paragraph (indefiniteness). In particular, the Examiner contends that the metes and bounds of the term "stable" are not clear because there is no indication of the level of stability required in the claims. Applicants traverse.

The meaning of the term "stable" is known in the art. For example, the applicants describe in the specification that RSV is unstable, and, as proof, point to its inactivation in less than three months when stored at -65°C to -86°C (paragraph [0004] of U.S. Patent Application Publication No. US 2008/0206281). Applicants also refer to the relative stability of virus compositions frozen at, for example, -1°C per minute or -2°C per minute as compared to virus compositions frozen at -0.3°C per minute (see, *e.g.*, Table 3-6) and to the relative stability of virus compositions frozen in bulk with liquid nitrogen as compared to in a lyophilizer (see, *e.g.*, Table 8). The level of stability of the viral composition, thus, is not indefinite. However, solely to expedite allowance of the instant application, applicants have amended claim 1 to recite that the lyophilized virus composition has a one-year potency loss of less than about a 17.6% log PFU loss as compared to the lyophilized virus composition before storage. Claim 24 recites that the lyophilized virus composition has less than about a 0.5 log PFU loss relative to the virus composition before lyophilization. Accordingly, applicants respectfully request that the Examiner withdraw the indefiniteness rejection.

Claims 1, 3, 5, 6, 8, 11, 13, 18, 22-25, 30, 33, 35, 37, 41, and 42 stand rejected under 35 U.S.C. § 112, first paragraph (written description). In particular, the Examiner contends that Tannock GA et al., Journal of Clinical Microbiology 25:1769-1771 (1987) ("Tannock") "teaches" that different strains of RSV have different stability after freeze drying. The Examiner further contends that the specification "fails to provide adequate teaching under the quid pro quo doctrine", and that applicants' teaching is not

commensurate with the scope of the claims in that, in the Examiner's view, the application does not teach how to freeze dry metapneumovirus, PIV1, or PIV2. Applicants traverse.

Applicants note that although the rejection is stated to be for lack of written description, the rejection includes statemenets that usually relate to enablement. Applicants, thus, will address both written description and enablement. Claims 1 and 24, the only independent claims in the rejected group, recite methods for producing a storage stable or lyophilization stable virus composition, respectively. These virus compositions comprise any of five types of viruses (RSV, PIV, mumps virus, measles virus, or metapneumovirus), or a combination thereof. The application as filed demonstrates the production of storage stable compositions involving two of the five viruses: RSV and PIV. All of the viruses belong to the paramyxoviridae family of viruses. The viruses exemplified, thus, share a similar genome structure, a similar physical structure, and a similar reproductive cycle in a host cell as mumps virus, measles virus, and metapneumovirus. Having exemplified two of the five recited virus types, and given the similarities within the group, applicants have provided sufficient representative members to meet the written description requirement for the recited viruses. The application as filed teaches methods for freeze drying two paramyxoviruses. The Examiner seems to read Tannock as teaching that freeze-drying will not stabilize some strains of RSV. Tannock says no such thing. Indeed, all of the strains tested in Tannock appear to be stabilized by freeze-drying. The Examiner, thus, has provided no reasoned basis for doubting applicants' claimed methods as required for a rejection based on enablement. Accordingly, applicants respectfully request that the Examiner withdraw the written description rejection.

35 U.S.C. § 102

Claims 1, 3, 5, and 6 stand rejected as allegedly anticipated by Tannock. In particular, the Examiner asserts that Tannock refers to a stabilized freeze dried RSV sample in SPGA buffer. Although the Examiner concedes that Tannock "is silent on the exact time of the freezing to glass transition temperature", the Examiner contends that "the Patent Office lacks the facilities to perform comparisons between the claimed material and prior art materials" and that applicants must distinguish the claimed product from the alleged prior art product. Applicants traverse.

Applicants respectfully request clarification from the Examiner regarding the anticipation rejection, and the opportunity to address the Examiner's concerns. Claim 1 and, by dependency, claims 3, 5, and 6 are directed to methods, not to products. To be anticipatory, a reference must disclose each and every limitation of the claim. Claim 1 recites freezing in 60 minutes or less. The Examiner concedes that Tannock does not refer to a time for freezing a virus composition below its glass transition temperature. Tannock, thus, does not teach each and every limitation of the claims. Claim 1 recites a freezing rate of -0.5°C to -2.5°C per minute. Tannock makes no mention of any freezing rate. Still further, claim 1 recites that the composition produced by the method of claim 1 loses less than about a 17.6% log PFU loss after at least one year at a storage temperature of about 1°C to about 10°C as compared to the lyophilized virus composition before storage. Tannock, thus, lacks disclosure of at least three limitations of claim 1. Accordingly, Tannock cannot anticipate the rejected claims. Applicants respectfully request that the Examiner withdraw the anticipation rejection.

35 U.S.C. § 103

Claims 1, 3, 5, 6, 8, 11, 18, 22-25, 30, 33, 35, 41, and 42 stand rejected as allegedly obvious over Tannock and Parrington M et al., International Application Publication No. WO 02/09749 ("Parrington"). In particular, the Examiner asserts that Tannock "teaches" a 0.5 ml stabilized freeze dried RSV sample in SPGA buffer using a commercial freeze-drying system, wherein the freeze-drying is done under vacuum, nitrogen is added to the chambers, and the ampoule is sealed. The Examiner concedes that Tannock does not teach a variety of buffers or freeze-drying conditions. The Examiner points to Parrington's alleged recitation of buffers and a freezing rate of -2°C per minute to remedy this defect. Applicants traverse.

The Examiner concedes that Tannock alone does not render obvious the pending claims. The Examiner's combination of Parrington and Tannock also fails. Parrington is directed to freeze-dried compositions of RSV proteins, not to freeze-dried compositions of an RSV virus. Contrary to the Examiner's assertion, there would have been no motivation to modify a method for freeze-drying a virus with steps for freeze-drying a protein. Nor would there have been any reasonable expectation of success even if one were motivated to do so. Paramyxoviruses are composed of RNA and a number of different proteins packaged in a viral envelope. One would, therefore, appreciate that viruses are significantly more complex than isolated proteins and would not expect methods for freezing one to be applicable to the other.

Claims 13 and 37 stand rejected as allegedly obvious over the combination of Tannock, Parrington, Suzuki M, Journal of Hygiene 68, 29-41 (1970) ("Suzuki"), and Heidemann R, Cytotechnology 32:157-167 (2000) ("Heidemann"). In particular, the Examiner relies on Suzuki to "teach" that peptone stabilizes freeze-dried smallpox and Heidemann to "teach" that soy peptone was available at the time of filing. The Examiner concludes that it would have been obvious to one of skill in the art to use soy peptone in the alleged method of Tannock and Parrington for stabilizing a freeze-dried virus. Applicants traverse.

As described above, the Examiner's combination of Tannock and Parrington fails to render the pending claims obvious. Any alleged recitation of peptone or soy peptone in Suzuki and Heidemann does not remedy this defect. Accordingly, applicants respectfully request that the Examiner withdraw the obviousness rejection.

CONCLUSION

In view of the foregoing evidence and arguments, Applicants respectfully submit that claims 1, 3, 5, 6, 8, 11, 13, 18, 22-25, 30, 33, 35, 37, 41-43, 46, 48-50, 54, 55, 60-63, 86, 105, and 122-124 are in condition for allowance. A Notice of Allowance is respectfully requested.

Respectfully submitted,

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